Citation:

Hibbeln JR, Davis JM, Steer C, Emmett P, Rogers I, Williams C, Golding J. Maternal seafood consumption in pregnancy and neurodevelopmental outcomes in childhood (ALSPAC study): an observational cohort study. *Lancet.* 2007 Feb 17;369(9561):578-85.

PubMed ID: 17307104

Study Design:

Prospective Cohort Study

Class:

B - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

The purpose of this observational cohort study was to assess a child's development including prosocial behavior, fine motor, communication, social development, and intelligence quotient based on different levels of maternal seafood intake during pregnancy.

Inclusion Criteria:

Pregnant women living in Bristol, UK, and surrounding areas, with an anticipated delivery date between April 1, 1991 and December 31, 1992.

Exclusion Criteria:

None described in article.

Description of Study Protocol:

Recruitment Avon Longitudinal Study of Parents and Children (ALSPAC). See Golding *et al*. Pediatr Perinat Epidemiol 2001;15:74-87.

Design Prospective cohort design

Blinding used (if applicable) not applicable

Intervention (if applicable) not applicable

Statistical Analysis

- Iterative curve-fitting analyses including linear, power, exponential, quadratic, and logarithmic analyses were used to assess the relationship of three categories of omega-3

intake to each outcome measure to estimate dose-response.
- Multivariate logistic regression analyses were used to assess relationships between seafood intake and outcome measures, while accounting for confounding variables.

Data Collection Summary:

Timing of Measurements

- Mothers were sent postal questionnaires four time during pregnancy and then at specific time points after the child's birth (6, 8, 30, 42, and 81 months).
- Children's IQ was measured at 8 years.

Dependent Variables

- Gross motor, fine motor, communication, and social skills scales, derived from the Denver Developmental Screening Test. Completed by the mother at home for their children at ages 6, 18, 30, and 42 months.
- The Strengths and Difficulties Questionnaire which included five subscales (prosocial, hyperactivity, emotional symptoms, conduct problems, and peer problems scales) and a total difficulties score. Completed by the mothers for their children at age 81 months.
- Intelligence quotient (IQ) was estimated with an abbreviated form of the WISC-III, which was given to 8-year old children at the research clinical with standard testing procedures.

Independent Variables

- Maternal seafood consumption measured by a self-completed, non-quantitative, detailed food-frequency questionnaire (FFQ) were obtained at 32 weeks' gestation.
- Validation of the FFQ against two different direct biochemical markers are described.

Control Variables

In total, controlled for 28 confounding variables including:

- 14 social & demographic variables: family adversity index, measure of parenting, sex of child, age of mother, parity, highest maternal education, educational attainment, housing status, stressful life events, had a partner at time of birth, smoking status during pregnancy, alcohol use during pregnancy, breastfeeding, and ethnicity
- 2 Perinatal variables: low birthweight and preterm delivery
- 12 dietary food groups

Description of Actual Data Sample:

Initial N: This study included participants in the Avon Longitudinal Study of Parents and Children (ALSPAC). Of 14541 pregnancies, 13988 children survived for at least 12 months. About 85% of eligible expectant mothers participated.

Attrition (final N): n=8946 at baseline, n=8801 at 81 months, n=5449 at age 8. (Details regarding attrition are not provided in the methods, but the discussion eludes to a disproportionate attrition of socially disadvantaged participants).

Age: approximately 3% less than 20 years of age, 97% greater than or equal to 20 years of age

Ethnicity: approximately 98% White, 1% Black, 1% Asian

Other relevant demographics:

Anthropometrics

Location: Bristol, UK, and surrounding areas

Summary of Results:

Key Findings:

- After adjustment, maternal seafood intake during pregnancy of less than 340 g per week was associated with increased risk of their children being in the lowest quartile for verbal intelligence quotient (no seafood consumption, odds ratio = 1.48, 95% confidence interval: 1.16 - 1.90, some seafood consumption, odds ratio = 1.09, 95% confidence interval: 0.92 - 1.29, overall P for trend = 0.004), compared with mothers who consumed more than 340 g per week.
- Low maternal seafood intake was also associated with increased risk of suboptimum outcomes for prosocial behavior, fine motor, communication, and social development scores.
- For each outcome measure, the lower the intake of seafood during pregnancy, the higher the risk of suboptimum developmental outcome.

Seafood Consumption:

- During pregnancy 12% were eating no fish, 65% were eating 1-340 g per week, and 23% more than 340 g per week
- Low seafood consumption was more likely in homes with evidence of social disadvantage (high level of family adversity, crowding, low maternal education levels, not being a home owner, and being a single parent) and less than ideal lifestyles (smoker, low parenting scores, and not breastfeeding)

Suboptimal Behavior, Development and IQ Scores by Maternal Seafood Consumption:

- Unadjusted odds ratio data consistently show that children of mothers who ate >340 g per week of seafood had outcomes that were not worse than children of women who 1-340 g per week; however, children of mothers who reported no seafood intake often had the greatest risk of suboptimum outcomes as indicated by trend tests. Furthermore, the trend tests and figures illustrate when seafood intake was moderate (1-340 g per week) the risk for suboptimum outcomes in the children were between those of no seafood consumption and those eating more than 340 g per week.
- Greater maternal intake of seafood was associated with lower risk of suboptimum verbal IQ in a non-linear dose-response curve. This same protective dose-response pattern was seen for nearly all outcomes significant in unadjusted and adjusted analyses.
- After adjusting for all 28 confounding variables, consumption of seafood in pregnancy was significantly associated with 9 of 23 outcomes. In each case, the higher the maternal seafood intake the less likely the infant was to have a suboptimum score.

Other findings:

- Fish oil supplements were consumed by 1.7% of participants, but a detailed analysis of fish oil supplements was not performed. The outcomes of infants of mothers who took

supplements, but did not eat seafood were close to those mothers who did eat fish.

Author Conclusion:

Maternal seafood consumption of less than 340 g per week in pregnancy did not protect children from adverse outcomes; rather, the authors showed beneficial effects on child development with maternal seafood intakes of more than 340 g per week.

The authors note no evidence to lend support to the warnings of US advisory groups that pregnant women should limit their seafood intake.

Reviewer Comments:

8-year cohort study with good retention rates. An extensive number of important confounding variables are included, and results of both adjusted and unadjusted models are reported. Authors note the following limitations:

- *No information about specific species of seafood or portion sizes*
- *Maternal reports of child development and behaviour are prone to reporting bias*
- *Disproportionate attrition of socially disadvantaged participants*

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions

1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions

1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes

1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	N/A
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	Yes
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	Yes
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	Yes
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	Yes
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	Yes

4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	Yes
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	N/A
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	Yes
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	N/A
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	Yes
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes

7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
8.6.	Was clinical significance as well as statistical significance reported?	Yes
8.7.	If negative findings, was a power calculation reported to address type 2 error?	N/A
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**	Yes
9.1.	Is there a discussion of findings?	Yes
9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**	Yes
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	Yes